

WHAT IS CLAIMED IS:

1. A composition for administration to a patient that is useful in photodynamic therapy in the patient, said composition comprising a carrier and a plurality of light-emitting nanoparticles that emit light having a first wavelength which activates a photodynamic therapy drug which absorbs light of said first wavelength, said light-emitting nanoparticles being present in said carrier in a quantity that is effective to activate said photodynamic therapy drug upon illumination with light from a light source emitting a second wavelength of light.
2. A composition according to claim 1, wherein said light emitting nanoparticles fluoresce upon absorption of two photons of activating light.
3. A composition according to claim 1 further comprising a therapeutically effective amount of said photodynamic therapy drug.
4. A composition according to claim 1 that emits multiple wavelengths of light within a waveband, wherein at least a portion of said light emitting nanoparticles are formed of a first light-emitting material and have different particle sizes.
5. A composition according to claim 1 that emits multiple wavebands of light, wherein a first portion of said light emitting nanoparticles are formed of a first light-emitting material and have different particle sizes that generate first wavelengths of a first waveband, and a second portion of said light emitting nanoparticles are formed of a second light-emitting material and have different particle sizes that generate second wavelengths of a second waveband.
6. A composition according to claim 1, wherein at least a portion of said plurality of light-emitting nanoparticles individually further comprise a target-specific component.
7. A conjugate according to claim 6, wherein the target-specific component is a first member of an affinity binding set, wherein said first

member is capable of selectively binding to a second member of the affinity binding set.

8. A conjugate according to claim 7, wherein the affinity binding set is selected from the group consisting of: biotin-avidin; biotin-streptavidin; antibody-antigen; antibody fragment-antigen; chemokine-chemokine receptor; and growth factor-growth factor receptor.

9. A mixture of light emitting nanoparticles adapted for use in photodynamic therapy, wherein said mixture comprises a first plurality of light-emitting nanoparticles that absorb light at a first wavelength and emit light at a second wavelength; a second plurality of light-emitting nanoparticles that absorb light at a third wavelength and emit light at fourth wavelength, said fourth wavelength differing from said second wavelength; and a carrier that is suitable to administer to a human patient; wherein said first plurality of light-emitting nanoparticles is present in said carrier in a sufficiently large number to activate a first PDT drug molecule upon administration to said patient; and wherein said second plurality of light-emitting nanoparticles is present in said carrier in a sufficiently large number to activate a second PDT drug molecule upon administration to said patient.

10. A conjugate for administration to a patient that is useful in photodynamic therapy in the patient, said conjugate comprising a light-emitting nanoparticle linked to a photodynamic therapy drug.

11. A conjugate according to claim 10, wherein said nanoparticle fluoresces upon absorption of two photons of activating light.

12. A conjugate providing sufficient illuminance to activate a photosensitive drug, said conjugate comprising a plurality of light-emitting nanoparticles linked to a polymeric backbone.

13. A conjugate according to claim 12, wherein said conjugate further comprises a target-specific component.

14. A method for photodynamic therapy, comprising:

administering a therapeutically effective amount of a photosensitive drug to a treatment area, wherein said photosensitive drug absorbs light of a first wavelength;

- administering a therapeutically effective quantity of light-
- 5 emitting nanoparticles to said treatment area, wherein said nanoparticles absorb light of a second wavelength and emit light of said first wavelength and wherein said therapeutically effective quantity of the light-emitting nanoparticles provides sufficient light of the first wavelength upon irradiation with light of the second wavelength to cause
- 10 the photosensitive drug to effect said therapy; and

illuminating the treatment area with light from a light source that emits light of said second wavelength, thereby causing the light-emitting nanoparticles to emit light of the first wavelength.

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15. A method according to claim 14, wherein the photosensitive compound is selected from the group consisting of indocyanine green; methylene blue; toluidine blue; aminolevulinic acid; phthalocyanines; porphyrins; texaphyrins; bacteriochlorins; merocyanines; psoralens; benzoporphyrin derivatives; porfimer sodium and its pro-drugs; α -aminolevulinic acid; protoporphyrin; chlorin compounds; purpurins; mono-,
- 20 di-, or polyamide aminodicarboxylic acid derivatives of cyclic or non-cyclic tetrapyrroles; alkyl ether derivatives of pyropheophorbide-a with N-substituted cyclic imides; derivatives of mono-L-aspartyl chlorin e6 (NPe6); pheophorbides and pyropheophorbides; porfimer sodium; omeprazole; benzoporphyrin verteporfin; hepatoporphyrin derivatives; and
- 25 dihematoporphyrin ether.

16. A method according to claim 14, wherein the nanoparticles fluoresce upon absorbing two photons of said light of said second wavelength.

17. A method according to claim 14, wherein the nanoparticles
- 30 are linked to a polymer backbone.

18. A method according to claim 14, wherein the light source is selected from the group consisting of a laser diode and a light emitting diode.

19. A method according to claim 14, wherein the light source
5 comprises a laser coupled to an optical fiber.

20. A method according to claim 14, wherein the light source comprises a light emitting diode array focused with a lens system.

21. A method according to claim 20, wherein the lens system comprises a totally internally reflecting lens.

10 22. A method according to claim 14 wherein the act of illuminating the treatment area with light from said light source that emits said light of said second wavelength, thereby causing the light-emitting nanoparticles to emit said light of the first wavelength, comprises:

15 illuminating a total internal reflection lens with said light from the light source and illuminating the nanoparticles with light transmitted by the total internal reflection lens.

23. A method according to claim 22, wherein the total internal reflection lens receives said light from the light source in an area of said lens having first cross-sectional area and transmits said light from the
20 lens over an area greater than the first cross-sectional area.

24. A method according to claim 22, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area less than the first cross-sectional area.

25 25. A method according to claim 14 wherein the act of illuminating the treatment area with light from said light source that emits said light of said second wavelength, thereby causing the light-emitting nanoparticles to emit said light of the first wavelength, comprises:

30 illuminating a total internal reflection lens with the light of the first wavelength generated by the nanoparticles, and illuminating the treatment area with light transmitted by the total internal reflection lens.

26. A method according to claim 25, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area greater than the first cross-sectional area.

5 27. A method according to claim 25, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area less than the first cross-sectional area.

10 28. A method for photodynamic therapy, comprising administering a therapeutically effective amount of a conjugate to a patient, wherein said conjugate comprises a light-emitting nanoparticle linked to a photosensitive compound.

29. A method according to claim 28, wherein the nanoparticle fluoresces upon absorbing two photons of activating light.

15 30. A method for photodynamic therapy, comprising:
administering a therapeutically effective amount of a photosensitive compound to a patient; and
administering a biocompatible matrix composed of a solid material to a treatment area of said patient, wherein said matrix includes
20 a therapeutically effective quantity of nanoparticles.

31. A method according to claim 30, wherein at least a portion of said quantity of nanoparticles fluoresces upon absorbing two photons of light of a first wavelength.

25 32. An illumination system for activating a photodynamic therapy drug, said illumination system comprising
a) a light source;
b) an optical fiber positioned to receive light generated by the light source and transmit said light toward an end of the optical fiber; and

- c) a total internal reflection lens positioned so that said lens receives light from the optical fiber and transmits light from said lens.

33. An illumination system according to claim 32 wherein said illumination system further comprises light-emitting nanoparticles that emit light having a first wavelength when illuminated by light of a second wavelength, said nanoparticles being positioned in an optical path of the illumination system such that said illumination system emits said light having the first wavelength.

34. An illumination system according to claim 33, wherein said nanoparticles are positioned to be illuminated by the light from the optical fiber.

35. An illumination system according to claim 33 wherein said nanoparticles are unitary with said optical fiber.

36. An illumination system according to claim 33 wherein said total internal reflection lens is positioned to receive said light from said nanoparticles across a first cross-sectional area of said lens and said total internal reflection lens transmits light from a second cross-sectional area of said lens, said first cross-sectional area being greater than said second cross-sectional area.

37. An illumination system according to claims 35 wherein said total internal reflection lens is positioned to receive said light from said nanoparticles across a first cross-sectional area of said lens and said total internal reflection lens transmits light from a second cross-sectional area of said lens, said first cross-sectional area being greater than said second cross-sectional area.

38. An illumination system according to claim 33 wherein said total internal reflection lens is positioned to receive said light from said nanoparticles across a first cross-sectional area of said lens and said total internal reflection lens transmits light from a second cross-sectional area

of said lens, said first cross-sectional area being less than said second cross-sectional area.

39. An illumination system according to claim 35 wherein said total internal reflection lens is positioned to receive said light from said
5 nanoparticles across a first cross-sectional area of said lens and said total internal reflection lens transmits light from a second cross-sectional area of said lens, said first cross-sectional area being less than said second cross-sectional area.

40. An illumination system according to claim 33, wherein said
10 nanoparticles are positioned to be illuminated by the light transmitted from the total internal reflection lens.

41. An illumination system according to claim 40 wherein said total internal reflection lens is positioned to receive said light from said nanoparticles across a first cross-sectional area of said lens and said total
15 internal reflection lens transmits light from a second cross-sectional area of said lens, said first cross-sectional area being greater than said second cross-sectional area.

42. An illumination system according to claim 40 wherein said total internal reflection lens is positioned to receive said light from said
20 nanoparticles across a first cross-sectional area of said lens and said total internal reflection lens transmits light from a second cross-sectional area of said lens, said first cross-sectional area being less than said second cross-sectional area.

43. An illumination system for activating a photodynamic
25 therapy drug, said illumination system comprising:

- a) a light source adapted to transmit light of a second wavelength to a treatment site of a patient; and
- b) a quantity of nanoparticles that emit light having a first wavelength upon illumination by said light source.

30 44. An illumination system according to claim 43 wherein said illumination system further comprises a total internal reflection lens which

receives light of said second wavelength to transmit said light to said nanoparticles.

45. An illumination system according to claim 43 wherein said illumination system further comprises a total internal reflection lens which
5 receives a light of said first wavelength to transmit said light to said treatment site.

46. An illumination system according to claim 43 wherein said light source comprises an optical fiber that transmits said light having the first wavelength to the treatment site.

10 47. A kit for photodynamic therapy in a patient, wherein the kit comprises a packaged combination of light-emitting nanoparticles that emit light of a first wavelength when illuminated by light of a second wavelength and an optical fiber which transmits light of said second wavelength.

15 48. A kit for photodynamic therapy in a patient, wherein the kit comprises a packaged combination of light-emitting nanoparticles that emit light of a first wavelength when illuminated by light of a second wavelength and a first photodynamic therapy drug that is activated by the light of the first wavelength.

20 49. A kit according to claim 48 wherein the kit further comprises a second photodynamic therapy drug that is activated by the light of the second wavelength.

50. A kit according to claim ~~47~~ and further comprising a set of instructions on use of the kit.

25 51. A composition according to claim 1, wherein said light-emitting nanoparticles comprise quantum rods.

52. A composition according to claim 1, wherein said light-emitting nanoparticles comprise TiO_2 .

30 53. A composition according to claim 1, wherein said light-emitting nanoparticles produce light having a sufficient illuminance at a

wavelength of less than 600 nm to activate said photodynamic therapy drug.

54. A composition according to claim 1, wherein said light-emitting nanoparticles produce light having a sufficient illuminance at a wavelength of less than 500 nm to activate said photodynamic therapy drug.

55. A composition according to claim 1, wherein said light emitting nanoparticles absorb light having a wavelength greater than 600 nm.

56. A composition according to claim 1, wherein said light emitting nanoparticles absorb light having a wavelength greater than 700 nm.

57. A composition according to claim 1, wherein said light emitting nanoparticles absorb light having a wavelength greater than 800 nm.

58. A composition according to claim 1, wherein said light emitting nanoparticles fluoresce upon absorption of two photons of activating light.

59. A composition according to claim 1 further comprising a therapeutically effective amount of said photodynamic therapy drug.

60. A composition according to claim 1, wherein said carrier comprises a biocompatible liquid.

61. A composition according to claim 1, wherein said carrier comprises a film.

62. A composition according to claim 1, wherein said carrier comprises a biodegradable polymer.

63. A composition according to claim 1 that emits multiple wavelengths of light within a waveband, wherein at least a portion of said light emitting nanoparticles are formed of a first light-emitting material and have different particle sizes.

64. A composition according to claim 1 that emits multiple wavebands of light, wherein a first portion of said light emitting nanoparticles are formed of a first light-emitting material and have different particle sizes that generate first wavelengths of a first

5 waveband, and a second portion of said light emitting nanoparticles are formed of a second light-emitting material and have different particle sizes that generate second wavelengths of a second waveband.

65. A composition according to claim 1, wherein at least a portion of said plurality of light-emitting nanoparticles individually further
10 comprise a target-specific component.

66. A conjugate according to claim 65, wherein the target-specific component is a first member of an affinity binding set, wherein said first member is capable of selectively binding to a second member of the affinity binding set.

15 67. A conjugate according to claim 66, wherein the affinity binding set is selected from the group consisting of: biotin-avidin; biotin-streptavidin; antibody-antigen; antibody fragment-antigen; chemokine-chemokine receptor; and growth factor-growth factor receptor.

Sub 20 68. A mixture according to claim 69, wherein said first wavelength and said third wavelength are equal.

69. A mixture according to claim 9, wherein the difference between said first wavelength and said third wavelength is no more than 300 nm.

25 70. A mixture according to claim 9, wherein said carrier comprises a biocompatible liquid.

71. A mixture according to claim 9, wherein said carrier comprises a solid material.

72. A mixture according to claim 71, wherein the solid material comprises a biodegradable material.

73. A mixture according to claim 9, wherein said mixture further comprises said first PDT drug molecule and said second PDT drug molecule.

74. A mixture according to claim 73, wherein said first PDT drug molecule and said second PDT drug molecule are identical.

75. A mixture according to claim 9, wherein each member of at least a portion of said first plurality of light-emitting nanoparticles individually has a delivery moiety.

76. A mixture according to claim ~~9~~, wherein at least a portion of said first plurality of light-emitting nanoparticles are attached to a polymer.

77. A conjugate according to claim ~~10~~, wherein said nanoparticle is linked to said photodynamic therapy drug through a target-specific component.

78. A conjugate according to claim 77, wherein the target-specific component is a first member of an affinity binding set, wherein said first member is capable of selectively binding to a second member of the affinity binding set.

79. A conjugate according to claim 78, wherein the affinity binding set is selected from the group consisting of: biotin-avidin; biotin-streptavidin; antibody-antigen; antibody fragment-antigen; chemokine-chemokine receptor; and growth factor-growth factor receptor.

80. A conjugate according to claim 10, wherein the nanoparticle and the photosensitive drug are individually linked to a polymeric backbone.

81. A conjugate according to claim 80, further comprising at least one additional nanoparticle to provide a plurality of nanoparticles in said conjugate.

82. A conjugate according to claim 81, wherein said plurality of nanoparticles provides light of sufficient illuminance to activate said photosensitive drug.

83. A method according to claim 14, wherein the nanoparticles comprise quantum rods.

84. A method according to claim 14, wherein the nanoparticles are a portion of a film that is administered to the treatment area.

5 85. A method according to claim 14, wherein the nanoparticles are incorporated into liposomes.

86. A method according to claim 14, wherein the nanoparticles are incorporated into nanocapsules.

10 87. A method according to claim 86, wherein the nanocapsules have a target-specific component.

88. A method according to claim 87, wherein the target-specific component is located on outer surfaces of the nanocapsules and comprises a first member of an affinity binding set, wherein said first member is capable of selectively binding to a second member of the affinity binding set.

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89. A method according to claim 88, wherein the affinity binding set is selected from the group consisting of: biotin-avidin; biotin-streptavidin; antibody-antigen; and antibody fragment-antigen.

20 90. A method according to claim 14, wherein the nanoparticles are composed of a biocompatible material.

91. A method according to claim 90, wherein the biocompatible material comprises TiO_2 .

92. A method according to claim 14, wherein the nanoparticles are linked to a target-specific component.

25 93. A method according to claim 92, wherein the target-specific component is a first member of an affinity binding set, wherein said first member is capable of selectively binding to a second member of the affinity binding set.

30 94. A method according to claim 93, wherein the affinity binding set is selected from the group consisting of: biotin-avidin; biotin-streptavidin; antibody-antigen; and antibody fragment-antigen.

95. A method according to claim 14, wherein the second wavelength is greater than about 600 nm.

96. A method according to claim 95, wherein the second wavelength is greater than about 700 nm.

5 97. A method according to claim ~~95~~, wherein the second wavelength is greater than about 800 nm.

98. A method according to claim 14, wherein the act of illuminating the treatment area consists essentially of introducing light of said second wavelength subcutaneously at the treatment area.

10 99. A method according to claim 14, wherein the act of illuminating the treatment area comprises irradiating an external portion of the patient's body at the treatment area with light of the second wavelength.

15 100. A method according to claim 98, wherein the light source is selected from the group consisting of a laser diode and a light emitting diode.

101. A method according to claim 98, wherein the light source comprises a laser coupled to an optical fiber.

20 102. A method according to claim 101, wherein the light source further comprises a light-diffusing tip positioned at an end of the optical fiber that is inserted into the patient.

103. A method according to claim 102, wherein the diffusing tip is cylindrical.

25 104. A method according to claim 15, wherein the light source comprises a light emitting diode array focused with a lens system.

105. A method according to claim 104, wherein the lens system comprises a totally internally reflecting lens.

106. A method according to claim 28, wherein the conjugate further comprises a linked target-specific component.

30 107. A method according to claim 106, wherein the target-specific component is a first member of an affinity binding set, wherein

said first member is capable of selectively binding to a second member of the affinity binding set.

108. A method according to claim 107, wherein the affinity binding set is selected from the group consisting of: biotin-avidin; biotin-streptavidin; antibody-antigen; and antibody fragment-antigen.

109. A method according to claim 30, further comprising illuminating the treatment area with light having a first wavelength which causes the nanoparticles to emit light having a second wavelength that activates the photosensitive compound.

110. A method according to claim 30, wherein the biocompatible matrix is biodegradable.

111. A method according to claim 30, wherein the biocompatible matrix is composed of polylactide.

112. A method according to claim 30, wherein the biocompatible matrix is administered by inserting said matrix into the patient's body.

113. A method according to claim 30, wherein both the photosensitive compound and the nanoparticles form part of the biocompatible matrix.

114. A method for photodynamic therapy according to claim 30, wherein the act of administering the biocompatible matrix comprises inserting a polymeric sheath into said patient's body, said polymeric sheath having proximal and distal ends and having nanoparticles incorporated on or in the polymeric material of which the sheath is composed, such that the distal end is located in proximity to the treatment area after insertion.

115. A method according to claim 114, further comprising illuminating the treatment area with a light source that emits light having a first wavelength which causes the nanoparticles to emit light having a second wavelength that activates the photosensitive compound.

116. A method according to claim 115, wherein the polymeric sheath contains a removable needle.

117. A method according to claim 116, further comprising delivering the photosensitive compound to the treatment area by injecting it into the patient's body and in proximity to the treatment area through the removable needle.

5 118. A method according to claim 116, wherein the method further comprises removing the needle after insertion of the polymeric sheath into the patient, and wherein the light source comprises a fiber optic light source that is inserted into the sheath from the proximal end of the sheath to the distal end.

10 119. A method according to claim 14 wherein the act of illuminating the treatment area with light from said light source that emits said light of said second wavelength, thereby causing the light-emitting nanoparticles to emit said light of the first wavelength, comprises:
 15 illuminating a total internal reflection lens with said light from the light source and illuminating the nanoparticles with light transmitted by the total internal reflection lens.

20 120. A method according to claim 119, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area greater than the first cross-sectional area.

25 121. A method according to claim 119, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area less than the first cross-sectional area.

30 122. A method according to claim 14 wherein the act of illuminating the treatment area with light from said light source that emits said light of said second wavelength, thereby causing the light-emitting nanoparticles to emit said light of the first wavelength, comprises:
 illuminating a total internal reflection lens with the light of the first wavelength generated by the nanoparticles, and illuminating the treatment area with light transmitted by the total internal reflection lens.

123. A method according to claim 122, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area greater than the first cross-sectional area.

5 124. A method according to claim 122, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area greater than the first cross-sectional area.

10 125. A method according to claim 28 wherein the act of illuminating the treatment area with light from said light source that emits said light of said second wavelength, thereby causing the light-emitting nanoparticles to emit said light of the first wavelength, comprises: illuminating a total internal reflection lens with said light from the light source and illuminating the nanoparticles with light transmitted by the
15 total internal reflection lens.

126. A method according to claim 125, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area greater than the first cross-sectional area.

20 127. A method according to claim 125, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area less than the first cross-sectional area.

128. A method according to claim 28 wherein the act of
25 illuminating the treatment area with light from said light source that emits said light of said second wavelength, thereby causing the light-emitting nanoparticles to emit said light of the first wavelength, comprises: illuminating a total internal reflection lens with the light of the first wavelength generated by the nanoparticles, and illuminating the
30 treatment area with light transmitted by the total internal reflection lens.

129. A method according to claim 128, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area greater than the first cross-sectional area.

5 130. A method according to claim 128, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area greater than the first cross-sectional area.

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10 131. A method according to claim 30 wherein the act of illuminating the treatment area with light from said light source that emits said light of said second wavelength, thereby causing the light-emitting nanoparticles to emit said light of the first wavelength, comprises: illuminating a total internal reflection lens with said light from the light source and illuminating the nanoparticles with light transmitted by the
15 total internal reflection lens.

132. A method according to claim 131, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area greater than the first cross-sectional area.

20 133. A method according to claim 131, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area less than the first cross-sectional area.

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25 134. A method according to claim 30 wherein the act of illuminating the treatment area with light from said light source that emits said light of said second wavelength, thereby causing the light-emitting nanoparticles to emit said light of the first wavelength, comprises: illuminating a total internal reflection lens with the light of the first wavelength generated by the nanoparticles, and illuminating the
30 treatment area with light transmitted by the total internal reflection lens.

135. A method according to claim 134, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area greater than the first cross-sectional area.

- 5 136. A method according to claim 134, wherein the total internal reflection lens receives said light from the light source in an area of said lens having a first cross-sectional area and transmits said light from the lens over an area greater than the first cross-sectional area.

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